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PTO/SB/30 (09-03)
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Request for Continued Examination (RCE) Transmittal

Address to:
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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Application Number	09/978,454
Filing Date	October 15, 2001
First Named Inventor	Erion et al.
Art Unit	1616
Examiner Name	Dameron Jones
Attorney Docket Number	45198.00027.RCE2(CON1)

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. See Instruction Sheet for RCEs (not to be submitted to the USPTO) on page 2.

1. Submission required under 37 CFR 1.114 Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).
   - a. ☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.
     - i. ☐ Consider the arguments in the Appeal Brief or Rely Brief previously filed on ______
     - ii. ☐ Other ______
   - b. ☑ Enclosed
     - i. ☑ Amendment/Reply
     - ii. ☐ Affidavit(s)/ Declaration(s)
     - iii. ☑ Information Disclosure Statement (IDS)
     - iv. ☑ Other Form PTO/SB/08A, with 25 references

2. Miscellaneous
   - a. ☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of ______ months. (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)
   - b. ☐ Other ______

3. Fees The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.
   - a. ☑ The Director is hereby authorized to charge the following fees, or credit any overpayments, to Deposit Account No. 50-2613
     - i. ☑ RCE fee required under 37 CFR 1.17(e)
     - ii. ☐ Extension of time fee (37 CFR 1.136 and 1.17)
     - iii. ☐ Other ______
   - b. ☑ Check in the amount of $ 770.00 enclosed
   - c. ☐ Payment by credit card (Form PTO-2038 enclosed)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

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01 FC:1801 770.00 OP

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Name (Print/Type)	Diana L. Bush, Ph.D., Esq.	Registration No. (Attorney/Agent)	51,109
Signature	Diana L. Bush	Date	January 30, 2004

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450 or facsimile transmitted to the U.S. Patent and Trademark Office on the date shown below.

Name (Print/Type)	Kimila Carraway		
Signature	Kimila Carraway	Date	January 30, 2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Erion *et al.*	
Serial No.: 09/978,454	Group Art Unit: 1616
Filed: October 15, 2001	Examiner: Dameron Jones
Title: NOVEL PRODRUGS FOR PHOSPHORUS-CONTAINING COMPOUNDS	

REMARKS

MAIL STOP RCE
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

These remarks accompany the filing of an RCE under 37 CFR 1.114. It is believed that no additional fee is required, but the Commissioner is hereby authorized to charge Deposit Account No. 50-2613 for any fees that may become due or credit become payable during the pendency of this application.

CERTIFICATE OF MAILING
(37 C.F.R. §1.8a)

I hereby certify that this paper (along with anything referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as First Class Mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

January 30, 2004
Date of Deposit
SAN/81752.1

Kimila Carraway
Name of Person Mailing Paper

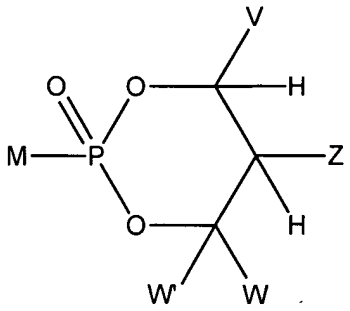
Kimila Carraway
Signature of Person Mailing Paper

Claims:

A complete set of all claims previously submitted, including the status for each claim, immediately follows below.

1.-167. (Cancelled)

168. (Previously added) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

V, W and W' are independently selected from the group consisting of hydrogen, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein the cyclic group optionally contains one heteroatom and is substituted with a hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy group attached to a carbon atom that is three atoms away from both oxygen atoms that are attached to the phosphorus atom; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group wherein the cyclic group optionally contains one heteroatom, and is fused to an aryl group, at the beta and gamma position to the oxygen attached to the phosphorus; or

together V and W are connected via an additional three carbon atoms to form an optionally substituted cyclic group containing six carbon atoms and is optionally substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy groups, wherein such substituent is attached to one of said carbon atoms that is three atoms away from an oxygen attached to the phosphorus atom; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$(aryl), $-CH$(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OC(O)R^3$, $-OCO_2R^3$, $-SC(O)R^3$, $-SCO_2R^3$, $-NHC(O)R^2$, $-NHCO_2R^3$, $-CH_2NH$(aryl), $-(CH_2)_pOR^{12}$, and $-(CH_2)_pSR^{12}$;

R^2 is selected from the group consisting of R^3 and hydrogen;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of hydrogen, and lower acyl; and

p is an interger 2 or 3;

with the provisos that:

a) V, Z, W, and W' are not all hydrogen; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not hydrogen, alkyl, aralkyl, or alicyclic; and

M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a carbon, oxygen, or nitrogen atom, with the proviso that $M\text{-}PO_3^{2-}$ is not an FBPase inhibitor;

wherein said compound of Formula I is converted to MPO_3H_2 by human liver microsomes;

pharmaceutically acceptable salts of Formula I;

and a pharmaceutically acceptable excipient.

169. (Previously Amended) The pharmaceutical composition of claim 168, wherein MH is 9-(2-phosphonylmethoxyethyl)adenine (PMEA) or analogues thereof.

170. (Previously Amended) The pharmaceutical composition of claim 168, wherein MH is 9-(2-phosphonylmethoxyethyl)adenine (PMEA).

171. (Previously Amended) The pharmaceutical composition of claim 168, wherein MH is selected from penciclovir, 3TC, ACV, PMPA, araC, ribavirin, fludarabine, and 5-fluoro-2'-deoxyuridine.

172. (Previously Amended) The pharmaceutical composition of claim 168, wherein MH is radiolabelled 2'-deoxy-5-Iodouridine.

173. (Previously Amended) The pharmaceutical composition of claim 172 wherein MH is 2'-deoxy-5-^{131}I-iodouridine.

174. (Previously Amended) The pharmaceutical composition of claim 168, wherein V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

175. (Previously Amended) The pharmaceutical composition of claim 168, wherein the prodrug is in the *cis* configuration.

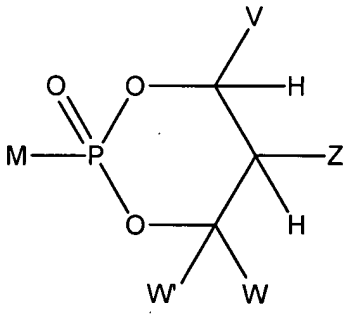
176. (Previously Amended) The pharmaceutical composition of claim 174, wherein the prodrug is in the *cis* configuration.

177. (Previously Amended) The pharmaceutical composition of Claim 171, wherein MH is araC and V is a heteroaryl group.

178. (Previously Amended) The pharmaceutical composition of claim 177, wherein V is 4-pyridyl.

179. (Previously Amended) The pharmaceutical composition of claim 172 wherein MH is 2'-deoxy-5-^{125}I-iodouridine.

180. (Previously added) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

V, W and W' are independently selected from the group consisting of hydrogen, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein the cyclic group optionally contains one heteroatom and is substituted with a hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy group attached

to a carbon atom that is three atoms away from both oxygen atoms that are attached to the phosphorus atom; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group wherein the cyclic group optionally contains one heteroatom, and is fused to an aryl group, at the beta and gamma position to the oxygen attached to the phosphorus; or

together V and W are connected via an additional three carbon atoms to form an optionally substituted cyclic group containing six carbon atoms and is optionally substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy groups, wherein such substituent is attached to one of said carbon atoms that is three atoms away from an oxygen attached to the phosphorus atom; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$(aryl), $-CH$(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OC(O)R^3$, $-OCO_2R^3$, $-SC(O)R^3$, $-SCO_2R^3$, $-NHC(O)R^2$, $-NHCO_2R^3$, $-CH_2NH$(aryl), $-(CH_2)_pOR^{12}$, and $-(CH_2)_pSR^{12}$;

R^2 is selected from the group consisting of R^3 and hydrogen;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of hydrogen, and lower acyl; and

p is an interger 2 or 3;

with the provisos that:

a) V, Z, W, and W' are not all hydrogen; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not hydrogen, alkyl, aralkyl, or alicyclic; and

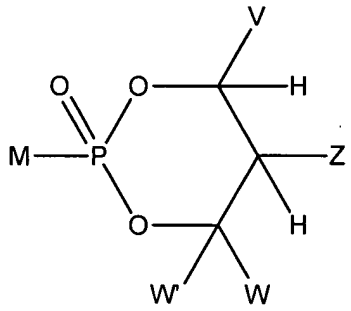
M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a carbon atom, with the proviso that MPO_3^{2-} is not an FBPase inhibitor;

wherein said compound of Formula I is converted to MPO_3H_2 by human liver microsomes;

pharmaceutically acceptable prodrugs and salts of Formula I;

and a pharmaceutically acceptable excipient.

181. (Previously added) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

V, W and W' are independently selected from the group consisting of hydrogen, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein the cyclic group optionally contains one heteroatom and is substituted with a hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy group attached to a carbon atom that is three atoms away from both oxygen atoms that are attached to the phosphorus atom; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group wherein the cyclic group optionally contains one heteroatom, and is fused to an aryl group, at the beta and gamma position to the oxygen attached to the phosphorus; or

together V and W are connected via an additional three carbon atoms to form an optionally substituted cyclic group containing six carbon atoms and is optionally substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy groups, wherein such substituent is attached to one of said carbon atoms that is three atoms away from an oxygen attached to the phosphorus atom; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$(aryl), $-CH$(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OC(O)R^3$, $-OCO_2R^3$, $-SC(O)R^3$, $-SCO_2R^3$, $-NHC(O)R^2$, $-NHCO_2R^3$, $-CH_2NH$(aryl), $-(CH_2)_pOR^{12}$, and $-(CH_2)_pSR^{12}$;

R^2 is selected from the group consisting of R^3 and hydrogen;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of hydrogen, and lower acyl; and

p is an interger 2 or 3;

with the provisos that:

a) V, Z, W, and W' are not all hydrogen; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not hydrogen, alkyl, aralkyl, or alicyclic; and

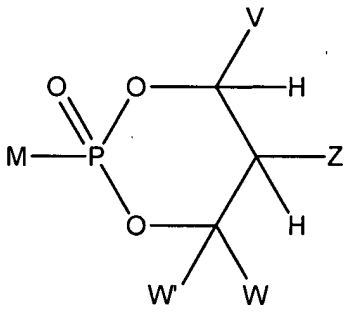
M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via an oxygen atom, with the proviso that MPO_3^{2-} is not an FBPase inhibitor;

wherein said compound of Formula I is converted to MPO_3H_2 by human liver microsomes;

pharmaceutically acceptable prodrugs and salts of Formula I;

and a pharmaceutically acceptable excipient.

182. (Previously added) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

V, W and W' are independently selected from the group consisting of hydrogen, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein the cyclic group optionally contains one heteroatom and is substituted with a hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy group attached to a carbon atom that is three atoms away from both oxygen atoms that are attached to the phosphorus atom; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group wherein the cyclic group optionally contains one heteroatom, and is fused to an aryl group, at the beta and gamma position to the oxygen attached to the phosphorus; or

together V and W are connected via an additional three carbon atoms to form an optionally substituted cyclic group containing six carbon atoms and is optionally substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy groups, wherein such substituent is attached to one of said carbon atoms that is three atoms away from an oxygen attached to the phosphorus atom; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$(aryl), $-CH$(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OC(O)R^3$, $-OCO_2R^3$, $-SC(O)R^3$, $-SCO_2R^3$, $-NHC(O)R^2$, $-NHCO_2R^3$, $-CH_2NH$(aryl), $-(CH_2)_pOR^{12}$, and $-(CH_2)_pSR^{12}$;

R^2 is selected from the group consisting of R^3 and hydrogen;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of hydrogen, and lower acyl; and

p is an interger 2 or 3;

with the provisos that:

a) V, Z, W, and W' are not all hydrogen; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not hydrogen, alkyl, aralkyl, or alicyclic; and

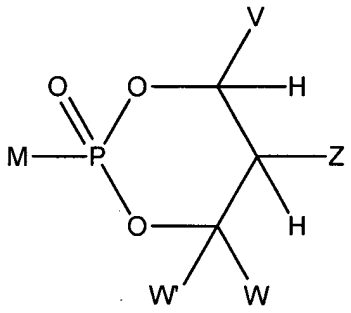
M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a nitrogen atom, with the proviso that MPO_3^{2-} is not an FBPase inhibitor;

wherein said compound of Formula I is converted to MPO_3H_2 by human liver microsomes;

pharmaceutically acceptable prodrugs and salts of Formula I;

and a pharmaceutically acceptable excipient.

183. (Previously amended) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

W and W' are independently selected from the group of H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

V is selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkynyl and 1-alkenyl;

Z is selected from $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$(aryl), $-CH$(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OC(O)R^3$, $-OCO_2R^3$, $-SC(O)R^3$, $-SCO_2R^3$, $-NHC(O)R^2$, $-NHCO_2R^3$, $-CH_2NH$(aryl), $-(CH_2)_pOR^{12}$, and $-(CH_2)_pSR^{12}$; or

together V and Z are connected via 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the oxygen attached to the phosphorus;

p is an integer 2 or 3;

R^2 is selected from the group of R^3 and –H;

R^3 is selected from the group of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of hydrogen, and lower acyl; and

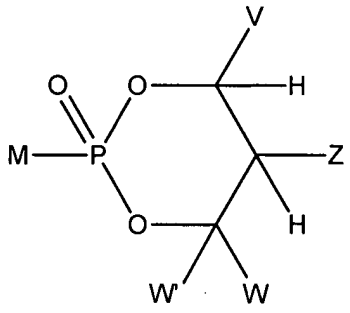
M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a carbon, oxygen, or nitrogen atom;

wherein said compound of formula I is converted to MPO_3H_2 by human liver microsomes, with the proviso that $M\text{-}PO_3^{2-}$ is not an FBPase inhibitor;

pharmaceutically acceptable prodrugs and salts of Formula I;

and a pharmaceutically acceptable excipient.

184. (Previously amended) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

V, W and W' are independently selected from the group of –H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

Z is selected from the group of: $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OCO_2R^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OC(S)OR^3$, –CH(aryl)OH, $-CH(CH{=}CR^2{}_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-SR^2$, $-CH_2NHaryl$, $-CH_2$ aryl; or

together V and Z are connected via 3-5 carbon atoms to form a cyclic group, optionally containing heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from an oxygen attached to phosphorus;

R^2 is selected from the group of R^3 and H;

R^3 is selected from the group of alkyl, aryl, alicyclic, and aralkyl; and

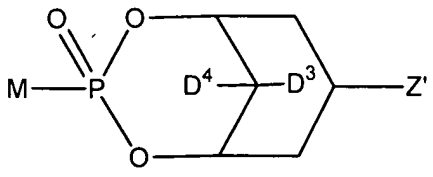
M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a carbon, oxygen, or nitrogen atom;

wherein said compound of formula I is converted to MPO_3H_2 by human liver microsomes, with the proviso that $M\text{-}PO_3^{2-}$ is not an FBPase inhibitor

pharmaceutically acceptable prodrugs and salts of Formula I;

and a pharmaceutically acceptable excipient.

185. (Previously amended) A pharmaceutical composition comprising a compound of Formula VIII:



VIII

wherein:

Z' is selected from the group of –OH, $-OC(O)R^3$, $-OCO_2R^3$, and $-OC(O)SR^3$;

D^4 and D^3 are independently selected from the group of –H, alkyl, $-OR^2$, –OH, and $-OC(O)R^3$; with the proviso that at least one of D^4 and D^3 are –H;

R^2 is selected from the group of R^3 and H;

R^3 is selected from the group of alkyl, aryl, alicyclic, and aralkyl; and

M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a carbon, oxygen, or nitrogen atom;

wherein said compound of formula I is converted to MPO_3H_2 by human liver microsomes, with the proviso that $M\text{-}PO_3^{2-}$ is not an FBPase inhibitor;

and pharmaceutically acceptable prodrugs and salts of Formula VIII;

and a pharmaceutically acceptable excipient.

REMARKS

Claims 168-185 have previously been allowed. The Applicants herewith submit a Supplemental Information Disclosure Statement for the Examiner's consideration.

The Applicants believe that the Application is in condition for allowance, and such action is respectfully requested at the Examiner's earliest convenience

Respectfully submitted,

Dated: 1/30/04

By: Diana L Bush

Diana L. Bush, Esq., Ph.D.
Reg. No. 51,109

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San Diego, CA 92130
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Facsimile: (858) 720-2555